

## A REVIEW ON PHYTOCHEMICAL ANALYSIS AND PHARMACOLOGICAL ACTIVITIES OF *ANNONA SQUAMOSA* LINN

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### ABSTRACT

In the present review, an attempt has been made to assemble the analysis of phytochemical and diverse pharmacological studies done on the *Annona squamosa* Linn. Medicinal plants and their formulations have been used since the period of human civilization to treat various ailments. The annonaceous acetogenins were the property of the expanding class of long chain fatty acid derivatives. This property is shown only by the annonacea family species. These compounds are high in demand due to their potential antitumor and antimicrobial activity with less harmful effect on human body. Based on numerous studies on *Annona squamosa* Linn, this review aims to synthesize information on its phytochemicals, folkloric applications, and bioactivities in an effort to advance knowledge of its medical benefits.

### I. INTRODUCTION

*Annona Squamosa* Linn. is a deciduous plant with a plethora of pharmacotherapy properties. The genus name, 'Annona' is from the Latin word 'anon', meaning 'yearly produce', referring to the production of fruits of the diverse species in this genus. The Annonaceae family, also known as the custard apple family. It is a tropical endemic species of the West Indies, Central and South America, Peru, Brazil and India (Kalidindi et al., 2015).

The ethanobotanical benefits conferred by the plant-based medicinal products surpassed their chemical counterparts owing to their lesser side effects and more positive outcomes. The all plant parts have various therapeutic properties, as well as being considered beneficial for ailments like cardiac disease, diabetes, hyperthyroidism, microbial infection and cancer [16]. Roots were found to be anticonvulsant effect (Vikas et al., 2017).

It has been discovered to have anti-tumor efficacy in both in vitro and in vivo investigations [7]. Fruit and fruit juice are used as astringents for diarrhea and dysentery as well as to treat worms and parasites, lower fevers, enhance postpartum milk production, and treat worms and parasites. Head lice, worms, and internal and external parasites are all treated with the crushed seeds. The bark, leaves, and roots are used to make a tea that is used for a variety of illnesses to counteract those effects, which are sedative, ulcer therapy, and nerve tonic. Acetogenins found in roots have been shown to have anti-carcinogenic effects via preventing DNA synthesis. Treatment for hysteria and fainting spells using leaves (Kaleem et al. 2008).

For diarrhea, a bark decoction is utilized. In dysentery, root extract can act as a good therapeutic medicine. Ice creams and milk beverages both contain fruits. Leaf decoction is used for gastritis, while crushed leaves are used for internal and external wounds and boils. Ripe fruits of plants are applied to malignant tumors to hasten suppuration, while vermin are destroyed by the use of its dried unripe fruit powder. The acrid and poisonous properties of seeds act as an insecticidal agent. Seed paste has been used in eradication of head lice, as well as destroying worms in the wounds of cattle [20]. Phytochemical studies have revealed that the custard apple contains numerous phenol-based compounds (proanthocyanidins) like alkaloids and flavonoids (Vradharajan et al., 2012).

Glycosides, Phytosterols, carbohydrates, oils, saponins, tannins, alkaloids, Phytosterols, carbohydrates, oils, saponins, tannins, alkaloids, phenols, flavonoids and diverse acetogenins compounds make this plant to exhibit activities such as anticancerous, antimicrobial, antidiabetic and antioxidant (Siegel et al., 2022).

**Taxonomical characterisation of *Annona squamosa* Linn.**(Cante and Garella,2021)



**Figure 1:**

Class : Magnoliopsida

order: Magnoliales

Family: Annonaceae Genus: Annona Species: Squamosa English: Custard apple

**Growth Form:** Small tree with an open, irregular crown.

**Foliage Leaves** are elliptic to oblong with rounded to acute apex (5-15 cm long, 2 - 5 cm wide). Leaves are alternate with entire leaf margins.

**Flowers:** Fragrant yellowish green flowers hang downwards either singly or in groups of 2 - 4. Each oblong flower has 3 elongated outer petals and 3 inconspicuous inner petals (2.5 - 4 cm long).

**Fruits** Fruit are usually round with a knobby surface. The sweet and juicy flesh occurs in elongated segments, each surrounding a brown to black, oblong seed (1 cm long). Each fruit has 20 - 40 seeds.

**Others - Plant Morphology Habitat:** Widely cultivated in the tropics for its fruit.

**Cultivation**

This species has good drainage and grows well in a variety of soil types. Apply a 3-10-10 NPK fertilizer to maximize fruit production. Propagate by seeds, grafting or budding. Propagation is mostly done by seeds. To maximize germination, remove the seeds from the pulp and let them dry for a week before sowing. Propagation by grafting can produce higher quality fruit in a shorter period of time than propagation by seeds. Susceptible to seed borers (*Bephratelloides cubensis*, *Bephratelloides maculicollis*, *Bephratelloides ruficollis*, *Bephratelloides paraguayensis*), scale insects (*Philephedra* sp.), beetles, mealybugs and fungal diseases (*Colletotrichum annonicola*, *Glomerella cingulata*)(Sigel et al.2022)

**Etymology** The genus "Annona" is the Latin American name for the harvest goddess. The species epithet "squamosa" is derived from the Latin word for scale or scale-like. The reference is to the immature fruit's scaly appearance.

**Ethnobotanical Uses** Edible Plant Parts (Edible Fruits)Food (Herb and Spice;Fruit & Vegetable)

**[Others]:** Food: The fruit is consumed raw. It is especially popular in Brazil and India. In Malaya, the fruit is added to milk and ice cream. Medicine: Bark extracts contain compounds that protect against cancer . In many parts of tropical America, a leaf decoction is used to treat colds and digestive / urinary ailments. Caution: Seeds contain toxic chemicals. A solution of ground seeds mixed with water may cause blindness upon contact with the eyes.[8].

**Nutritional value**

100 grams of edible portion of fruit consists of.[4]Vitamin C - 37gm

Calcium -17gm

Iron	- 4.37gm
Carbohydrate	- 23.5gm
Fibre	- 3.1gm

Protein	-1.6gm
Phosphorus	- 47gm
Fat	- 0.4gm
Energy-	- 104 Kcal

## II. PHYTOCHEMISTRY

Phytochemicals were extracted and separated using distilled water and 96% of ethanol. Qualitative phytochemical analysis was carried out using a method described by Trease and Evans Trease and Evans (1989). Each extract was analysed for the presence of alkaloids with Mayer's, Wagner's, Hager's and Dragendorff's reagents; flavonoids (NaCl and HCl); carbohydrates with Molisch's, Benedict's and Fehling's reagent; glycosides with Keller-Killiani and Borntrager's; protein and amino acids with Biuret, Xanthoproteic, Ninhydrin and Millon's reagent; tannin and phenolic compound (FeCl<sub>3</sub> and Gelatin); triterpenoid with thionylchloride; steroid and sterols with Liebermann-Burchard and Salkowski's reagents and fat and fixed oil with alcoholic KOH reagents (Padhi et al., 2011).

Pharmacologically active compounds such as alkaloids, tannins, coumarins, flavonoids, cardiac glycosides, carbohydrates, phenols and saponins were detected in the leaves of *Annona squamosa*. However, terpenoids and phlobatannins were absent (Cante and Garella, 2021).

The chemical constituents like anonaine, aporphine, coryline, isocorydine, norcorydine, glaucine. Leaves contain 4-(2-nitro-ethyl)-1-β-D-xylopyranosyl-1-β-D-glucopyranosyl-oxy)benzene, Anonaine, Benzyltetrahydroisoquinoline, Borneol, Camphene, Camphor, car-3-ene, Carvone, β-Caryophyllene, Eugenol, Farnesol, Geraniol, 16-Hetriacontanone, Hexacontanol, Higemamine, Isocorydine, Limonine, Linalool acetate, Menthone, Methyl anthranilate, Methylsalicylate, Methylheptenone, p-(hydroxybenzyl)-6,7-(2-hydroxy,4-hydro) isoquinoline, n-Octacosanol, α-Pinene, β-Pinene, Rutin, Stigmasterol, β-Sitosterol, Thymol and n-Triacontano, isolated from leaves, stems and roots of the plant (Neha Pandey).

*Annona squamosa* Linn. bark showed the presence of volatile oil and collected by the method of steam distillation and analysed using GC-MS. The oil showed significant antimicrobial activity against *Bacillus subtilis* and *Staphylococcus aureus* (Madhuri and G. Pandey, 2009).

The preliminary phytochemical tests showed that *Annona squamosa* seed extract contains terpenoids, alkaloids, coumarins, and flavonoids [11]. Numerous such substances are known to have strong anticancer effects. Terpenoids, flavonoids, alkaloids, and tannins are thought to have significant antioxidant activity and can either prevent or treat a variety of illnesses, including cancer (Alimzhanova et al., 2012).

**Table 1:** Preliminary Phytochemical screening of leaf extract of *Annona squamosa*. Constituents Pet ether ext chloroform ext methanol ext water ext

	Pet ether ext	chloroform ext	methanol ext	water ext
Steroids	+	+	-	-
Triterpine	-	+	-	-
Glycoside	+	+	+	+
Alkaloids	-	-	+	+
Flavonoids	-	-	+	+
Saponins	-	-	+	+
Phinolic compounds	+	+	+	+

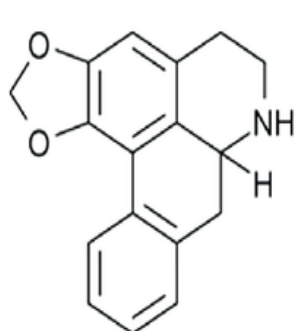
+ Present

\_ Absent

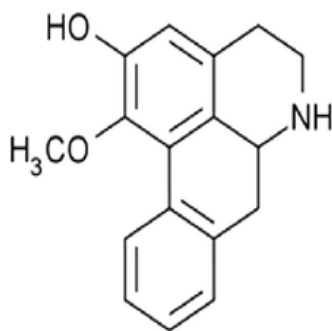
**Table 2:** List of various chemical constituents present in various parts of *Annona squamosa* Linn.

S.No	Constituents isolated	Parts
1	Anonaine Anolobine Aporphine Corydine Isocorydine Norcorydine Glaucine Liriodenine Naulaureline	Leaves, tender stem, bark, roots, seeds, roots Roots Leaves, tender stem Leaves, tender stem, bark Leaves, tender stem, bark Leaves, Tender stem Leaves, Tender stem, Bark RootsRoots
2		
3		
4		
5		
6		
7		
8		
9		
10	NorushinsunineReticuline Annosqualine	LeavesRoots Stem
11		
12		

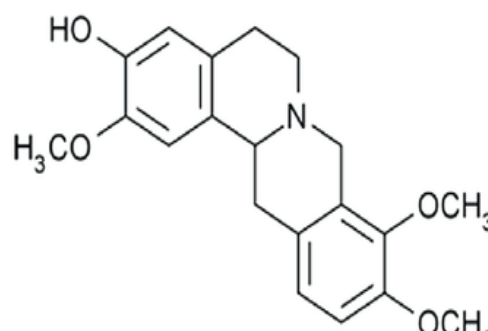
**Constituents isolated**



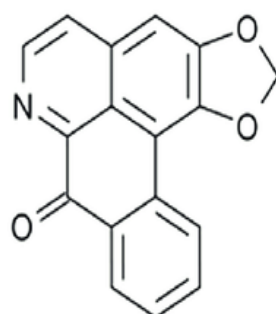
Anonaine



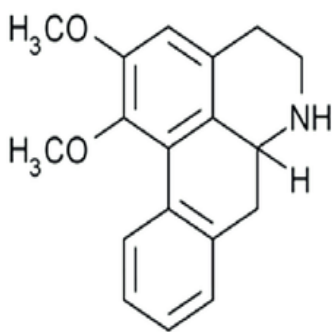
Asimilobine



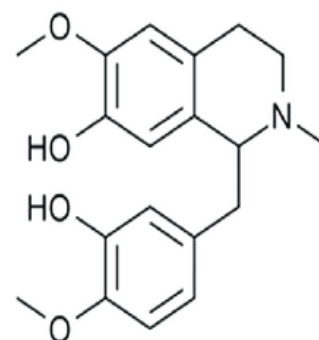
Corypalmine



Liriodenine



Nornuciferine



Reticuline

**Figure 2:**

Constituents isolated

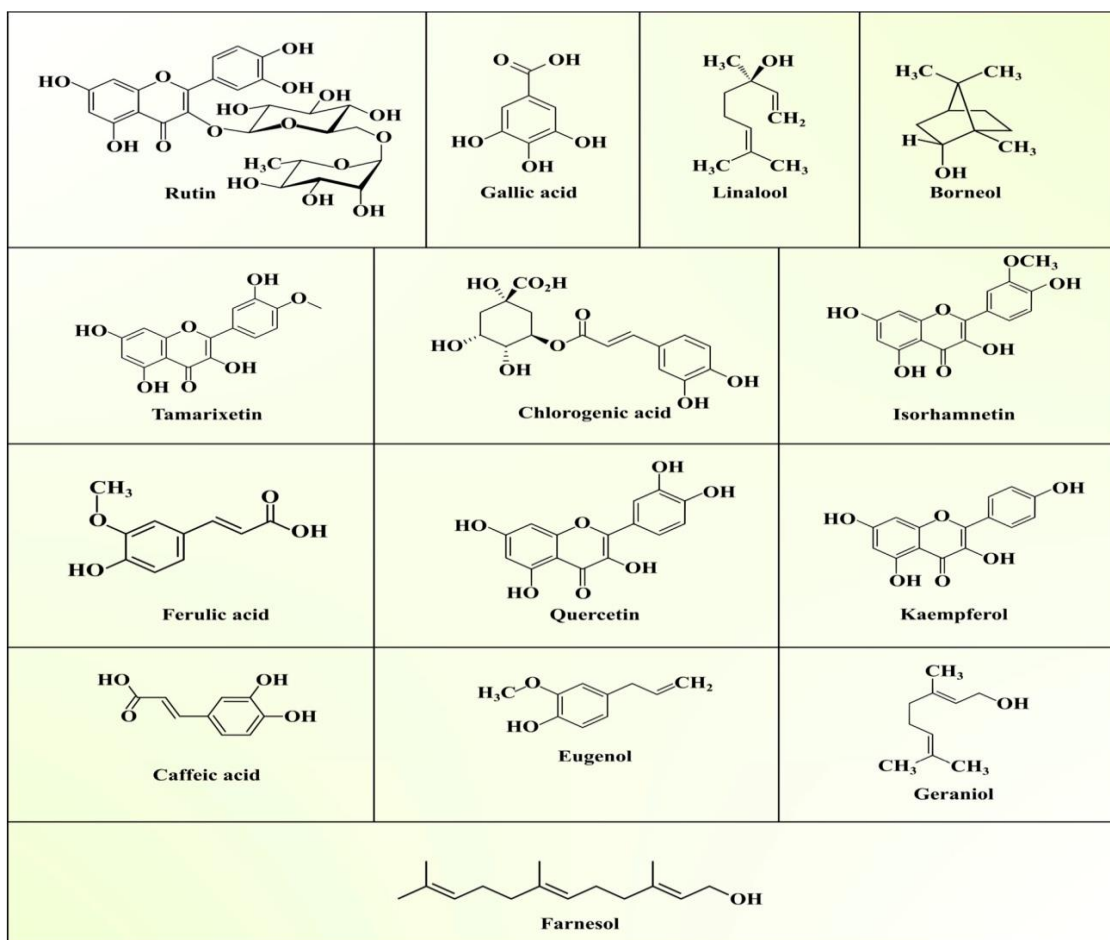


Figure 3

Pharmacological activities

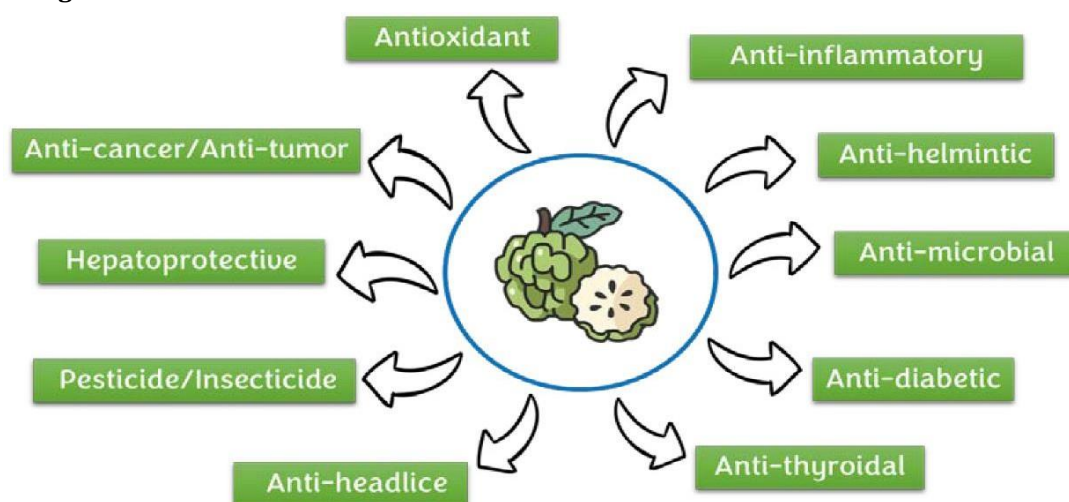


Figure 4

Antibacterial activity

The antibacterial activity of *Annona squamosa* extract was screened against *Bacillus subtilis* MTCC 7164, *Staphylococcus aureus* MTCC 1144, *Staphylococcus epidermidis* MTCC 3615, *Escherichia coli* MTCC 1098, *Salmonella typhimurium*, MTCC 3216, *Pseudomonas aeruginosa* MTCC 1034, *Vibrio cholerae* MTCC 3904 and *Vibrio alginolyticus* MTCC 4439 using agar cup method . The antibacterial action of the extraction is more



efficient on Gram-positive than on Gram-negative bacteria. According to the results of the agar cup antibacterial screening, the methanol extract of *Annona squamosa* leaf had the maximum zone of inhibition, followed by petroleum ether and aqueous extracts. All test microorganisms but *Salmonella typhimurium* had their growth suppressed by *Annona squamosa* extracts. The activity of aqueous extracts was lower than that of methanol extracts (Padhi et al., 2011).

#### Antidiabetic activity

Diabetes is a metabolic condition marked by a rapid rise in blood sugar levels. Diabetes mellitus is becoming more common worldwide, although it is especially prevalent in Asia. Along with insulin, a variety of oral hypoglycemic medications, including biguanides and sulfonylurea, are available for the treatment of diabetes mellitus (Cante and Garella, 2021). However, these human-induced medications have the potential to cause harmful side effects and should not be used while pregnant (Varadharajan et al., 2012).

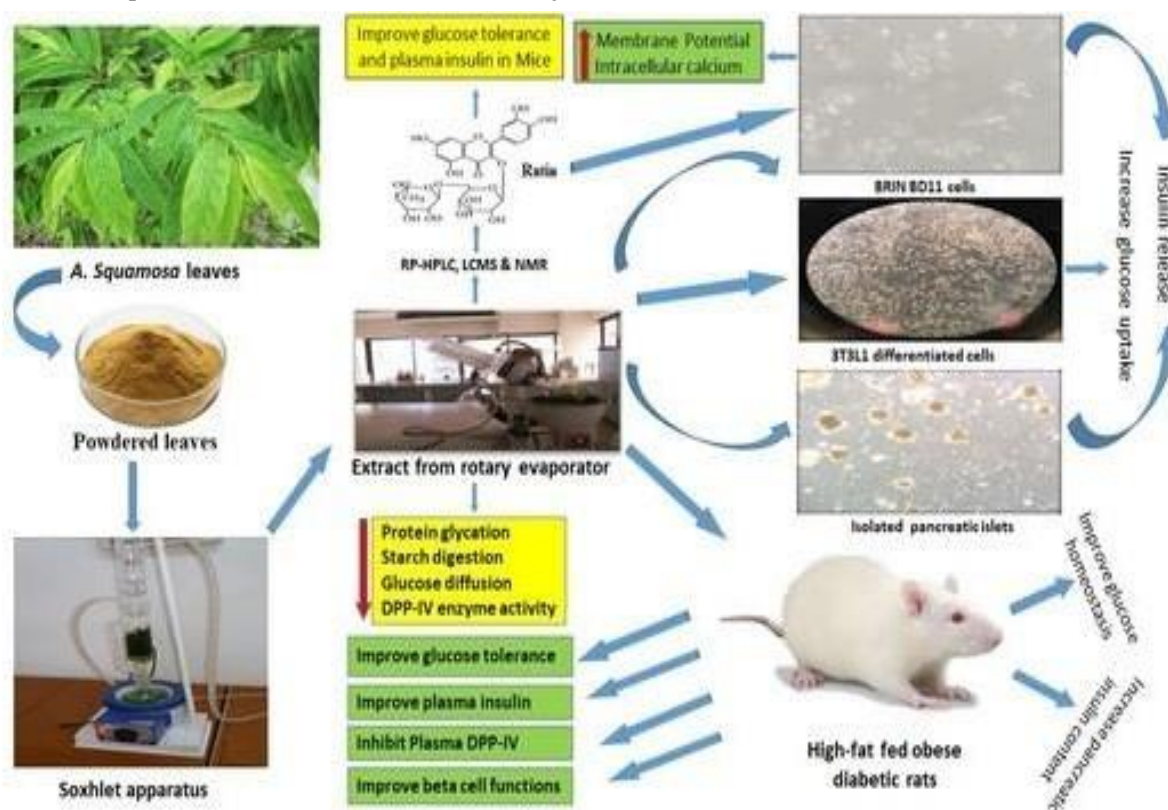
According to Latner (1958), the primary causes of hyperglycemia in diabetes mellitus are excessive production (excessive hepatic glycogenolysis and gluconeogenesis) and inadequate tissue uptake of glucose.

The antidiabetic activity of the *Annona squamosa* is particularly widespread and well-liked in the Lodha community, where the plant's fruit is considered as the source of nutrient compounds. The formula has been around since then and is currently being utilized by some allopathic and unani doctors (Abdel Hameed et al., 2012). Since ancient times, the utilization of young leaves of *Annona squamosa* combined with seeds of *Piper nigrum* for the curing of diabetes. The hot water extract of *Annona squamosa* leaves exhibits hypoglycemic and antidiabetic activity (Gupta et al., 2005).

Experimental studies were done on the alloxan-induced diabetic rats. Various doses of (2.5, 5.0, 10.0 g/kg b.w.) of *Annona squamosa* fruit pulp fed to the three groups were each of normal healthy and diabetic rats orally for one month. The control group of animal (normal and diabetic animal) also examined. Protein efficiency ratio (PER), digestibility coefficient (DC), biological value (BV) and net protein usage (NPU) were measured, as well as progress in the nutritional level was analysed by comparing it with the control group. Effect of the fruit pulp was also examined on various biochemical parameters, like fasting blood glucose (FBG), total cholesterol (TCH), HDL-cholesterol, triglyceride (TG), total protein (TPR), alkaline phosphatase (ALKP), serum glutamate oxaloacetate and pyruvate transaminases (SGOT and SGPT), serum creatinine (CRTN) and serum bilirubin (BIL). Protein and glucose in urine were also estimated. The feeding pulp animals showed positive results compared to the control animals. Its results for the liver and heart by recycling in the SGOT, SGPT, ALKP and serum bilirubin levels (Gupta et al., 2005).

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**Schematic representation of antidiabetic activity**



**Figure 5**

**Anticancerous activity**

Cancer is a devastating disease and the second highest mortality rate caused due to cancer in the United States, accounting for about 610,000 deaths in 2022[17]. Recent studies have focused on alternative therapies for cancer that do not involve the use of chemotherapy. Anticancerous drugs derived from plant sources have significant demand nowadays due to the least side effects. Moreover, they only target the cancer cells, without affecting normal cells(Abd-Elgany et al.,2022).

The presence of phytochemicals like terpenoids, flavonoids, glycosides, alkaloids and phenols have the antioxidant property that they quench the free radicals and they work as cancer-preventive agents(Wang z et al.,2016).

Due to the high surface area, efficient interaction articles can be utilised to target the delivery of therapeutic drugs. Niosomes can act as nanocarriers due to their low-cost, stable and biodegradable properties(Fahmy et al.,2021).

The MTT assay (mtc) colorimetric method was employed to measure cell proliferation against HeLa cells. This assay is based on the principle of reducing MTT (yellow tetrazolium salts) to formazan crystals (purple formazan crystals) by living mitochondria(Abdel -Hameed) This process involves the absorption of MTT into live cells and the reduction of MTT to formazan through succinate dehydrogenases in the mitochondrial electron transport chain(Cante R.c) The anticancer activity (IC50) of *A. squamosa* L. leaf isolate against HeLa cells was 70.9021 ppm, which belonged to the moderate cytotoxic category. *Annonas squamosa* seed oil contains unsaturated fat and Annonaceous Acetogenin, which effectively prevents the growth of H22 solid tumours. In the future it might help to development of novel cancer medicines(Alimazhanova.,2012).

Schematic representation of anticancerous activity

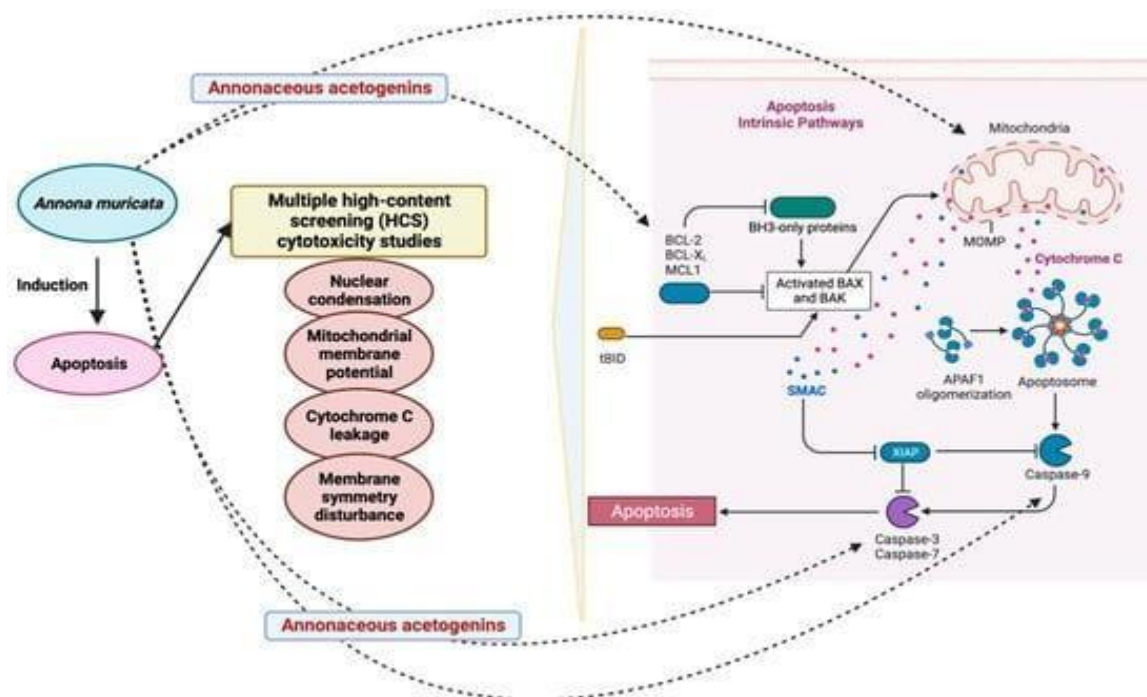


Figure 6

**Anti-arthritic, anti-inflammatory and analgesic activity**

Current research indicates that the plant contains potential anti-inflammatory components such as sterols, triterpenoids, flavonoids and tannins that may be useful in the development of botanical medicines to treat inflammation.. Complete Freund's Adjuvant (CFA) was injected into the metatarsal footpad of Sprague-Dawley rats to cause arthritis. The size of the hind paws and body weight were used to gauge the degree of inflammation, and the histopathology of the knee joint was used to estimate AST, ALT, and TP. The combined extract led to a notable reduction in paw volume, an increase in body weight, and a decrease in the elevated levels of ALT, AST, and TP. The animal treated with plant extract had significantly less neutrophil infiltration, pannus formation, and bone damage for anti-arthritic activity, according to the histopathological analysis. According to the extract, it has analgesic and anti-inflammatory properties(Raj Sobiya et al.,2009).

Further research is needed to establish the exact anti-inflammatory mechanism of action of Annona squamosa alcoholic extract(Yadav DK.,2021).

**Antiulcer activity**

1-4-D-GLUCOPYRANOSYLOXYMPHENYL (2-D-GLUCOPYRANOSYSTEMANO)-ETHANE

was extracted from the twigs/branches of plants of the Annona Squamosa species. Patients were screened for antulcer activity using cold restraint/aspirin-induced-pyloric-ligation models as well as alcohol-induced gastric ulcer/histamine-induced-duodenal ulcer models. Omeprazole was used as the standard drug after comparison of the results. The results of the evaluation indicated antulcer activity in vivo by decreased total acidity/pepsin in gastric-ligation models, confirmed by inhibition of h(+)/K(+)-ATPASE activity in vitro with corresponding reduction of plasma gastrin levels(Yadav DK.,2021).

**Antimalarial activity**

The significant activity of extracts from Annona squamosa cell carcinoma suggests these two actions. The plant has a strong insecticidal effect against insects, especially mosquitoes. A promising source of larvicides. This is some Medium polar compounds in the extract can act synergistically or competitively. Active website. Plants collected in Brazil showed larvicidal activity against Aedes aegypti and against C. quinquefasciatus and Anopheles. Results of current larval control activities supported the report and showed that extracts from Annona squamosa species have potential. Anti-mosquito drug. Recent studies on Annona squamosa have demonstrated all the compounds. Moderate activity against chloroquine-sensitive and chloroquine-resistant



strains Plasmodium falciparum(Kumar VA. And Girish C,2021).

### III. CONCLUSION

Alternative medication and natural remedies have been used from ancient times for the treatment and wellbeing of humans. The entire plant parts of the *Annona squamosa* have significant medicinal properties to treat diverse human ailments due to the highly therapeutic phytoconstituents present in them. Compared to modern medicine, the medicinal plant based therapies have least side effect as well as it can combine with some biotechnology techniques. Hence further studies and investigation required to understand the wide variety of modern applications of *Annona squamosa* Linn.

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